Appendix C

Detailed Comments on the Integrated Exposure Uptake Biokinetic Implementation Code

The uncertainties and inaccuracies listed below are referenced to sections of the Technical Support Document (TSD) for the integrated exposure uptake biokinetic (IEUBK) model (EPA 1994).

1. The bone weight (WTBONE, as given by equation B-5g (p. A-10 of the TSD) is not continuous, because the two equations do not match at 12 months with the given definition for WTBODY. At 12 months, 0.111 × WTBODY = 1.1192265, whereas 0.838 + (0.02 × 12) = 1.078, about 4% lower.

2. Equation B-2b (p. A-7 of the TSD) defines TRBCPL as

$$\text{TPLRBC} \times (\text{RATBLPL} - 0.55/[0.55 + 0.73]).$$

The text (p. 40 of the TSD) simply states that TRBCPL is the product of TPLRBC and RATBLPL minus a constant, without any explanation why. If TRBCPL is being estimated by the usual assumption that the ratio of TRBCPL and TPLRBC is equal to the steady-state mass ratio (p. 29, paragraph 2 of the TSD), then the "constant" here is not in fact quite a constant, because then:

$$\text{TRBCPL/TPLRBC} = \text{RATBLPL} - (\text{VOLPLASM/VOLBLOOD})/ ([\text{VOLPLASM/VOLBLOOD}] + [\text{VOLECF/VOLBLOOD}])$$

3. VOLECF/VOLBLOOD = 0.73 (equation B-5d of the TSD), but VOLPLASM/VOLBLOOD is not the constant 0.55 implied in equation

B-2b. Although this ratio is fairly constant, it is only as low as 0.55 for ages less than 0.4 month and exceeds 0.6 for all ages between 5 and 84 months (with the parameter values given in equations B-5a and B-5c). None of this makes any substantial difference, but the discussion on page 29 needs to be amplified to indicate where this "constant" comes from.

4. On the same matter, to agree with the statement that the ratio of times is equal to the ratio of steady-state masses (p. 29 of the TSD), it should not be the ratio of TRBCPL and TPLRBC that is set to this mass ratio but the ratio of TRBCPL to TPLRBC2, because TPLRBC2 is the actual-time constant.

5. The definition of TPLRBC2 given in equation B-2.5 of the TSD is not physical, since it relates to VOLRBC (t – 1), which presumably is supposed to be the volume of red blood cells at the previous time step, and, of course, the time step of a computer program has nothing to do with the mathematical definition of the problem. It might be a viable approximation in a computer program to use the value in the previous time step, but in the actual computer code, the value in the previous month is used not the value in the previous time step.[1]

6. On p. A-10 of the TSD, equations B-5a, B-5b, and B-5c define the blood, plasma, and red blood cell volumes, but the required relationship VOLBLOOD = VOLPLASM + VOLRBC does not hold at all times. It is not clear what the difference is supposed to represent. With the values given, this difference turns out to have different signs at different ages, suggesting that the equation just given is supposed to hold (as one would expect, unless there is supposed to be another compartment to hold the other cellular components of blood). This is an example of an unnecessarily introduced approximation that would be trivial to correct.

7. On p. B-7 of the TSD, a definition of HCT0 is given in such a way that numerically it differs from 1 – VOLRBC(0)/VOLBLOOD(0). This is again an unnecessary approximation.

8. On page A-18 of the TSD, the initial conditions are defined. However, the source of these initial conditions is not clear. The statement after equations B-7a through B-7d that equations B-7a through B-7d are "numerically equivalent to the following equations" is incorrect. For example, equation B-7d could be numerically equivalent to the corresponding equation below only for HCT0 = 1.284, which is physically impossible. B-7b could be numerically equivalent to its corresponding equation below only accidentally. Indeed, neither set of equations corresponds to the assump-

[1]The system requirements and design document for the IEUBK model (EPA 2002) indicate that *t* refers to the month (which corresponds to the code). As mentioned, use of the value from the previous time step would be a viable approximation, but instead the previous month is used.

tions described earlier in the TSD. If some other set of assumptions is being used, then it should be documented how those assumptions lead to the equations of p. A-18. In the computer code, both sets of equations are present, and indeed both are executed; but only the second has any effect.

9. On page A-19 of the TSD, equations B-7e and B-7l contradict the statements made under MCORT*(t)* on page B-9, and MTRAB*(t)* on page B-11. In both cases, it is stated that there is an assumption that the bone (cortical or trabecular) lead concentration/blood lead concentration ratio is equal to the bone (composite) lead concentration/blood lead concentration ratio (so cortical and trabecular bone lead concentration/blood lead concentration ratios should be equal). Equations B-73 and B-7l give different concentration ratios (78.9 for cortical, 51.2 for trabecular).

10. Equations B-4a through B-4d (p. A-9) are stated (p. B-4 and B-5) to come from an analysis of the data of Barry (1981). However, at age 0 they are contradicted by the initialization conditions given in equations B-7e through B-7l (p. A-17), which are said to be based on the same data (p. B-9, B-10, B-11). For kidney, liver, and other tissues, the tissue/blood concentration ratios implied by equations B-4a, B-4b, and B-4d at time 0 are 0.777, 1.1, and 0.931 L/kg, whereas equations B-7f, B-7g, and B-7h give 1.06, 1.30, and 1.60 L/kg, respectively. Here is another internal inconsistency, because equation B-4c gives a bone/blood concentration ratio of 6.0 L/kg at t = 0, whereas equations B-7e and B-7f give separate ratios at t = 0 of 7.89 and 5.12 L/kg for cortical and trabecular bone, respectively.

REFERENCES

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